

In the Claims

1-61 (canceled).

62 (new). An antibody that induces superagonistic signaling by a cell surface receptor, wherein said antibody binds to the extracellular portion of the receptor at a membrane proximal region and said receptor comprises a cytoplasmic domain which is dependent on an extrinsic protein kinase, wherein said antibody does not bind only the C'-D loop of human CD28.

63 (new). The antibody according to claim 62, wherein said antibody:

- (i) binds orthogonally to the main axis of the domain of the receptor which it is binding, and/or
- (ii) which lies parallel to the cell surface when bound to the receptor, and/or
- (iii) which binds to a β -strand polypeptide chain of the receptor, and/or
- (iv) which binds within 75Å of the cell surface.

64 (new). The antibody according to claim 62, wherein said receptor

- (i) comprises an ITAM motif, ITIM motif or “switch” signaling motif, and/or
- (ii) is a member of the CD28 family of proteins, and/or
- (iii) is expressed on the surface of a cell of the immune system, and/or
- (iv) comprises a cytoplasmic domain capable of being phosphorylated by a Src kinase, and/or
- (v) comprises a cytoplasmic domain capable of being dephosphorylated by CD45, and/or CD148, and/or another large receptor tyrosine phosphatase, and/or
- (vi) is one of the receptors listed in Table 2.

65 (new). The antibody according to claim 62, wherein said cell surface receptor is CD28, CTLA-4, ICOS, PD-1 or BTLA.

66 (new). The antibody according to claim 62, wherein said antibody binds to an epitope selected from:

<i>Protein</i>	
hPD-1	PALLVV; DNATF; RMSPSNQTDK; QPGQDCRFR; MSVVR; NDSGTY; LRAELR;
hBTLA	QSEHSI; DPFEL; KLNG; QTSWK; LHFEP; NDNGSY; TTLVVT;

<i>Protein</i>	
hCD28	SPMLV; AVNLS; SLHKGLDSAVEVCV; VYSKTGFNCDG; FYLQN; TDIYFC; NGTIHIV;
hCTLA-4	PAVVL; GIASFV; TVLRQADSQVTEVCA; FLDDSICTG; LTIQG; TGLYIC; NGTQIYV;
hICOS	YEMFI; GVQIL; QLLKGGQILCD; VSIKSLKFCHS; FFLYN; ANYYFC; TGGYLHI;

<i>Protein</i>	
hCD28	GNYSQQLQVYSKTGF; YMMGNELTFLDDS; KTKGSGNTVSIKSLK; or LAAFPEDRSQPGQDCR.
hCTLA-4	
hICOS	
hPD-1	